Clinical Nutrition ESPEN 57 (2023) 126–130

Contents lists available at ScienceDirect

Clinical Nutrition ESPEN

journal homepage: http://www.clinicalnutritionespen.com

Original article

A multi-national survey of experience and attitudes towards managing catheter related blood stream infections for home parenteral nutrition

Francisca Joly [a, *], Alexandre Nuzzo [a], Federico Bozzetti [b], Cristina Cuerda [c], Palle B. Jeppesen [d], Simon Lal [e], Georg Lamprecht [f], Manpreet Mundi [g], Kinga Szczepanek [h], André Van Gossum [i], Geert Wanten [j], Loris Pironi [k]

[a] Department of Gastroenterology and Nutritional Support, Center for Intestinal Failure, Reference Centre of Rare Disease MarDI, AP-HP Beaujon Hospital, University Paris Cité, Inserm UMR, Paris 1149, France
[b] Faculty of Medicine, University of Milan, Milan, Italy
[c] Departamento de Medicina, Universidad Complutense de Madrid, Nutrition Unit, Hospital General Universitario Gregorio Marañón, Madrid, Spain
[d] Department of Intestinal Failure and Liver Diseases, Rigshospitalet, Inge Lehmanns Vej 5 Opgang 3, 12. Og 16, Sal 2100, København Ø, Denmark
[e] Gastroenterology, Salford Royal & University of Manchester, UK
[f] Department of Medicine II, Division of Gastroenterology and Endocrinology, Rostock University, Medical Center, Rostock, Germany
[g] Division of Endocrinology, Diabetes, Metabolism, and Nutrition, Mayo Clinic, Rochester, MN, USA
[h] General and Oncology Surgery Unit, Stanley Dudrick's Memorial Hospital, Skawina, Poland
[i] Department of Gastroenterology and Clinical Nutrition, Hopital Erasme/Institut Bordet Brussels, Belgium
[j] Department of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen 6500 HB, the Netherlands
[k] Alma Mater Studiorum -University of Bologna, Department of Medical and Surgical Sciences, Italy IRCCS Azienda Ospedaliero-Universitaria di Bologna, Centre for Chronic Intestinal Failure - Clinical Nutrition and Metabolism Unit, Italy

ARTICLE INFO

Article history:
Received 7 February 2023
Accepted 23 June 2023

Keywords:
Intestinal failure
HPN
Short bowel syndrome
Central venous access
Central venous catheter
CRBSI

SUMMARY

Background and aims: Catheter-related bloodstream infection (CRBSI) is the most common complication of home parenteral nutrition (HPN) in patients with chronic intestinal failure (CIF). The aim of this study was to assess the broad range of practices of international multi-disciplinary teams involved in the care of this complication occurring in CIF patients.

Design: An online questionnaire was designed and distributed to members of the European Society for Clinical Nutrition and Metabolism (ESPEN) and distributed to colleagues involved in managing patients with CIF.

Results: A total of 47 responses were included from centers across 21 countries. The centers had been delivering HPN for a median 21 years (IQR 11–35) and were actively following a median 58 patients (27–120) per center for benign CIF in 80% of cases (67–95). Tunneled catheters were the most common type of central venous catheters (CVC), representing 70% (47–86) of all CVC in use. For the management of CRBSI, written procedures were provided in 87% of centers. First measures included simultaneous central and peripheral blood cultures (90%), stopping HPN infusion (74%), and administrating an antibiotic lock and systemic antibiotics (44%). Immediate removal of the CVC was more likely in case of fungal infection (78%), *Staphylococcus aureus* (53%), or in case of PICC catheter (52%) (all $p < 0.01$). After the first CRBSI, 80% of centers used preventive CVC locks (taurolidine in 84% of cases, $p < 0.001$). We observed a large heterogeneity in practices regarding preparation, duration, reaspiration, and volume of CVC locks, and monitoring of CRBSI (timing of blood cultures, radiological work-up).

Conclusion: In this international survey of HPN expert centers, we observed a significant consensus regarding the initial management of CRBSI and the use of secondary preventive CVC locks, while areas of variation exist. Management of CRBSI may be improved with clearer recommendations based on the micro-organism and the type of CVC, including PICC lines which are increasingly used yet insufficiently studied in HPN patients.

* Corresponding author. Gastroenterology, IBD and Intestinale Failure Department, Beaujon Hospital, Paris Cité University, France.
E-mail address: francisca.joly@aphp.fr (F. Joly).

https://doi.org/10.1016/j.clnesp.2023.06.032
2405-4577/

1. Introduction

Home parenteral nutrition (HPN) is the primary life-saving therapy for patients with chronic intestinal failure (CIF) due to either benign or malignant diseases. HPN may also be provided to patients in the late phases of end-stage diseases [1]. A central venous catheter (CVC) is required for sustained venous access. In general, the type of venous access device used can depend on a number of factors including the available expertise at the local center, as well as the predicted duration of HPN. As HPN patients usually receive therapy over a long period of time, tunneled catheters and infusion ports are mostly used. Peripherally inserted CVCs (PICCs) are only preferred if the estimated duration of HPN is limited. The most common venous access-related complications for HPN patients are infection, thrombosis and functional complications such as partial or total CVC occlusion. Catheter-related infections can include both local and systemic infections. Local infections include exit-site, tunnel and pocket infections, while generalized systemic infections include catheter-related bloodstream infection (CRBSI), which is the most common complication associated with the use of a CVC. CRBSI is associated with significant morbidity, including hospitalization and resultant healthcare expenditure, and unfortunately is also associated with mortality.

The first European Society for Clinical Nutrition and Metabolism (ESPEN) guideline on HPN was published in 2009 [2]. It consisted of 26 recommendations, 10 were based on some evidence (grade B recommendations) but 16 were mostly based on expert opinion ('grade C recommendations') [2]. The updated version of ESPEN guidelines on HPN care was commissioned in order to incorporate new evidence since the publication of the previous ESPEN guidelines. They consist of 71 recommendations on HPN indications, central venous access device (CVAD) and infusion pump, infusion line and CVAD site care, nutritional admixtures, program monitoring and management [1]. The aim was to provide recommendations to healthcare professionals on safe HPN administration, including CRBSI prevention using the most appropriate dressing, type of venous access, catheter handling, and antiseptic lock administration (recommendations 19 to 38). Guidelines relating to the management of CVC infections were published in 2009 and 2013 [3,4]. Recommendations concerning the treatment of CVAD infections were also included in these ESPEN guidelines [5], as well as in the ESPEN guidelines on CIF (recommendations 85,86) [6]. However, no studies have yet been carried out on impact of these guideline recommendations on CRBSI management on clinical practice protocols. The aim of our work was to collect clinical opinion regarding prevention, diagnosis and treatment of CRBSI, in order to assess the attitudes of clinicians involved in the care of this complication occurring in patients on HPN.

2. Methods

2.1. Survey

A fifty-seven-item questionnaire was designed to collect data regarding the use of CVCs, attitudes towards the management of suspected or confirmed CRBSI, as well as subsequent secondary prevention in HPN-dependent patients. The questionnaire was designed by members of the ESPEN specialist interest group for HPN and CIF, with individual questions written using medical education guidance for developing research surveys. The questionnaire evaluated respondents' demographics, experience with HPN, indications for HPN (CIF or cancer) and respondents' attitudes towards CRBSI. The online questionnaire was administered using Google forms. Drop down lists, binary (yes/no) and multiple-choice answers were utilized to allow objective assessment of answers and an 'Other, please comment' option was given for relevant questions. A full version of the survey is provided in the Appendix. Type of catheter was classified into 3 main groups: Tunneled catheters, Port catheters, and PICCs. Type of germ was classified into 4 groups: *Coagulase negative staphylococcus*, *Staphylococcus aureus, Gram negative bacilli, and Fungus.* The invitation to participate in the survey was circulated by an ESPEN newsletter to all ESPEN members and the answers were collected between September 2019 and May 2020.

2.2. Statistical analysis

Responses to the survey were downloaded from Google forms into Excel for further analysis. Categorical variables, expressed as counts (percentages) and frequency distributions were compared between type of catheters and germ groups using Chi square or Fisher exact tests, as appropriate. Continuous variables are expressed as medians [interquartile ranges (IQR)] and were compared between type of catheters and germ groups using Student t or Mann–Whitney U tests, as appropriate. All tests were two-sided. A p-value <0.05 was considered significant. No imputation of missing data was performed. All analyses were performed using the Statistical Package for the Social Sciences (SPSS) for Mac OSX software (version 23.0, Chicago, IL, USA) and R software, version 3.6.2 (R Foundation for Statistical Computing).

3. Results

3.1. Participating centers and catheter use

A total of 47 responses were included in the analyses from 47 centers across 21 countries over 4 continents: 2 (4%) responses from North America, 4 (9%) from South America, 1 (2%) from Australia, 1 (2%) from Asia and 39 (83%) from Europe. Within Europe, Spain returned the most responses (8, 21%), followed by France (7, 18%), Italy (6, 15%) and Poland (4, 9%) (see Table 1). The centers had been delivering HPN for a median 21 years (IQR 11–35) and were actively following a median 58 patients (27–120) for benign CIF in 80% of cases (67–95). Five centres were "recent centres" with a HPN program developed during the last 5 years. We can notice that 6 centers had less than 5 HPN patients per year. Tunneled catheters were the most common type of catheters used across centers (n = 42, 89%), representing 70% (47–86) of all catheters in use. Port catheters were used by 38 (81%) centers, representing 18% (6–40) of all catheters. PICCs were used by 30

Table 1
Geographic origin of the 47 participating centers.

Europe (n = 39)	America (n = 6)	Other (n = 2)
Spain (8)	USA (2)	Israel (1)
France (7)	Chile (1)	Australia (1)
Italy (6)	Mexico (1)	
Poland (4)	Brazil (1)	
Denmark (3)	Argentina (1)	
UK (2)		
Belgium (2)		
Slovenia (1)		
Norway (1)		
Netherlands (1)		
Germany (1)		
Serbia (1)		
Croatia (1)		
Portugal (1)		

The number of participating centers per continent and country is specified in brackets.

centers (64%), representing 29% (13–40). Arterio-venous fistulas were used in 6 centers (13%), representing 3% [3–6] of all catheters.

3.2. General management

In cases of fever occurring at home, several recommendations were provided to the patients. Patients were advised to stop HPN infusion in 74%, contact an HPN on-call staff member in 72%, disconnect the central line in 41%, and seek medical attention at the HPN center in 35%, via the emergency room in 28% or via the general practitioner in 11% of centers. These instructions for management at home were provided in writing, orally and/or online in 87%, 69% and 16% of centers, respectively.

3.3. CRBSI suspicion

When a CRBSI was suspected, the microbiological work-up included performing simultaneous central and peripheral blood cultures (90%), chest x-ray (54%), nasal swabs for *Staphylococcus aureus* detection (6%), and blood cultures after saline infusion into the catheter (4%) ($p < 0.001$). First therapeutic measures included stopping HPN infusion (74%), administrating an antibiotic lock and systemic antibiotics (44%) and providing systemic anticoagulation (8%). The first line curative locks are described on Table 2. The most commonly used catheter lock during an infection was vancomycin (58%, $p < 0.001$), followed by taurolidine (20%), gentamicin (16%), amikacin (11%), ethanol (6%) and a fibrinolytic agent (2%). No significant difference was found in the type of lock across the different type of catheters. The first lock was placed for at least 24 h in 37% of centers, 12 h in 26%, 48 h in 16%, and for more than 72h in 6% of centers, with no significant difference between the type of catheters.

3.4. Confirmed CRBSI

After a confirmed CRBSI, immediate removal of the catheter was significantly more likely in cases of fungal (78%) or *Staphylococcus aureus* infections (53%) ($p < 0.001$) (see Table 3). Immediate removal was also significantly more likely for PICCs (52%, vs. 32% of ports and 18% of tunneled catheters, $p < 0.01$) (see Table 3). When a lock was used, it was re-aspirated in 70% of centers, placed for at least 12 h in 54% of centers, and changed systematically (i.e. even if the catheter was not infused) every 24 h in 78% of centers. The most common duration of systemic antibiotic after CRBSI was around >7 days for coagulase negative staphylococcus (91%) and gram-negative bacilli (100%), >14 days for *Staphylococcus aureus* (71%) and fungal infection (100%), with no significant difference across the types of catheters. The monitoring of CRBSI included performing central venous blood cultures at the end of systemic antibiotics in 82% of centers (vs. 29% at 48 h and 22% at 72 h), echocardiography in 40%, venous ultrasonography in 9% and CT-scan in 6%.

3.5. Secondary prevention after CRBSI

After the first CRBSI, 79.5% of centers used preventative locks. Taurolidine was the most commonly used preventative lock (84% of cases, $p < 0.001$), followed by heparin in 10%, ethanol in 8%, vancomycin in 3% and gentamycin in 3%. The most common taurolidine concentration was the 1.35% taurolidine (Taurolock®) used by 77% of centers, or 2% taurolidine (Taurosept®) used by 23% of centers. No significant difference was found in the type of lock used among the different types of catheters. The main indication for offering preventative locks was after a first CRBSI in 41%, after more than one CRBSI in 30%, and only for high-risk patients in 29% of centers. The volume of the preventative lock was most commonly adapted to the type of catheter in 56% of centers; in other cases, a fixed volume was used routinely (3 ml and 6 ml in 39% and 10% of cases, respectively). The lock was prepared by nurses, the patient themselves or the pharmacist in 43%, 35% or 30% of cases, respectively.

4. Discussion

This work is a unique international survey collating the responses of HPN experts from 47 centers in 21 countries. The study reports the different practices from a very diverse range of international centers, facilitating identification of consensus and disparities in approaches to CRBSI management, as well as a clear description of unmet needs.

HPN is lifesaving in patients with CIF due to benign disease, but its use is also associated with the risk of infectious and noninfectious CVC-related complications. Of these, CRBSI is the most common and can lead to CVC removal. Multiple CVC removals are associated with venous stenosis and thrombosis which, in turn, can lead to the permanent loss of vascular access [7]. Furthermore, CRBSI is a potentially life-threatening complication, usually requiring hospital

Table 2
Type of curative lock used in case of CRBSI suspicion.

Curative Lock \ Catheter	Ports n = 36 (%)	Tunneled n = 47 (%)	PICC n = 35 (%)	*p-value*
vancomicine	18 (50)	23 (49)	16 (46)	0.93
amikacin	3 (8)	5 (11)	3 (9)	0.92
gentamicin	5 (14)	6 (13)	6 (17)	0.85
taurolidine	6 (17)	9 (19)	6 (17)	0.95
ethanol	3 (8)	3 (8)	3 (9)	0.92
fibrinolytic	1 (3)	1 (2)	1 (3)	0.97
p-value	<0.001	<0.001	<0.001	

Table 3
Immediate removal of the catheter for confirmed CRBSI according to the type of catheter and the type of infection.

Germ \ Catheter	Ports n = 40 (%)	Tunneled n = 40 (%)	PICC n = 35 (%)	*p-value*
Coagulase negative staphylococcus	8 (20)	2 (5)	14 (40)	<0.001
Gram negative bacilli	11 (28)	3 (8)	17 (49)	<0.001
Staphylococcus aureus	20 (50)	16 (40)	24 (68)	0.04
Fungus	31 (78)	32 (80)	30 (86)	0.65
p-value	<0.001	<0.001	0.001	

admission, with associated high costs for the healthcare system. A systematic review in adult patients receiving HPN showed an overall CRBSI range of between 0.38 and 4.58 episodes/1000 catheter days (median 1.31). Gram-positive bacteria of human skin flora caused more than half of these infections [8].

The impact that recurrent CVC removal can have on future venous access suggests that catheter salvage should be attempted wherever possible in HPN-dependent patients with CRBSI [7]. Catheter salvage is attractive because it obviates the inconveniences and risks of CVC replacement, especially in those patients who have limited remaining venous access or who cannot tolerate prolonged periods without HPN after catheter removal; on the other hand, catheter removal does reduce the risk of infection recurrence, persistent bacteremia and metastatic infection [7]. Whereas non-HPN/CIF guidelines recommend CVC removal in most cases of CRBSI, catheter salvage aims to retain the CVC with the use of appropriate catheter lock therapy and systemic antibiotics, usually for around 10–14 days, with the goal of maintaining long term venous access [4,9]. However, the appropriateness of catheter salvage in specific situations still remains a matter for debate [4,9–11].

Current European HPN guidelines recommend attempting CVC salvage solely in patients with uncomplicated infections arising from *Staphylococcus aureus*, coagulase-negative staphylococci (CNS) and Gram-negative bacilli [6]. In contrast, the Infectious Diseases Society of America (IDSA) guidelines advocate catheter removal or replacement as a first-line approach to CRBSI [4]. All guidelines agree on removing the CVC in patients who are hemodynamically unstable, for CRBSIs caused by yeasts, or in cases of complicated infections such as endocarditis, septic thrombosis and other metastatic infections [11]. The data presented in this paper demonstrate that clinicians currently tend to remove the CVC particularly in cases of fungal infections and to a lesser degree in patients with *Staphylococcus aureus* infections, in keeping with established guidelines.

There was wide use of lock therapy for CRBSI management in about half of the cases for tunneled catheters or PORTs, but locks were less frequently used for PICCs (32%). Notably, most preferentially used vancomycin locks ($p < 0.001$), in keeping with published practice [7]. However, practice varied as regards the duration and concentration of the antibiotic lock administered, as did the concomitant use of fibrinolytics. While heparin seems to have been frequently added as an anticoagulant to the lock solution in the published literature, the concentration and duration of lock solutions has varied significantly among studies to-date [7].

Furthermore, it is noteworthy that blood cultures were generally performed between 48 and 72 h at the end of treatment regardless of the type of CVC. While one-fifth of respondents reported using PICCs, there are limited established data on CRBSI management for these types of catheters, perhaps reflecting the frequent removal of these catheters compared to PORT and tunneled catheters. Thus, 40% of respondents stated that they systematically removed PICCs as compared to 20% for PORTs and 5% for tunneled catheters in the case of coagulase negative staph infections ($p < 0.04$).

It is currently established from the published literature that antimicrobial locks should be used in tandem with systemic antibiotics when managing CRBSIs. Indeed, a recent systematic review appraising the available evidence on CRBSI management in adult patients on HPN, focusing on the safety and efficacy of available CRBSI management approaches with successful catheter salvage as the outcome, demonstrated that to achieve successful catheter salvage, the addition of an antimicrobial lock solution was superior to systemic antibiotics alone (OR: 1.75; 95% CI: 1.21, 2.53; $P = 0.003$) [7]. Regarding systemic antibiotic therapy, our work shows an overall duration of 10–21 days depending on the organism. The type of administered systemic antibiotics varied considerably in the literature. Most studies mentioned empirical treatment according to IDSA guidelines with sensitivity-based adjustments [7]. However, in clinical practice, a number of questions remain regarding the use of antibiotic lock therapy for CRBSI management: what concentration of lock should be used? How should it be administered? Should it be changed every day? Can locks be prepared in advance? At the moment there are no commercially available antibiotic lock solutions and pharmacies do not regularly provide custom made solutions either. Additionally, standards of practice regarding concentration and conditioning have not been established, which may facilitate future studies and unify use.

Taurolidine locks were reported to be in wide use for secondary prevention of infections in more than 85% cases. After one or 2 infections, two-thirds of respondents systematically used preventative locks. This practice is consistent with ESPEN recommendations, and it is notable that this approach is now widespread and more standardized.

This study has some limitations. This work was a survey study, subject to respondents' selection bias and measurement accuracy errors. Nevertheless, although most respondents were from Europe, our study collected data across four continents, providing a unique insight into CRBSI management approaches and highlighting areas of consensus, disparities, and unmet needs.

5. Conclusion

We observed significant consensus regarding the initial management of CRBSI and the use of secondary preventative CVC locks (taurolidine), although areas of variation in practice still exist. Management of CRBSI may be improved with clearer recommendations based on the micro-organism and the type of CVC, including PICCs, which are increasingly used yet insufficiently studied in HPN patients.

Grants and funding

None.

Authors' contributions

Study concept and design: **FJ**, **AN**, **FB**, **LP**; acquisition of data: **AN**, **FJ**, **FB**, **LP**, **CC**, **PBJ**, **SL**, **GL**, **MM**, **KS**, **AVG**, **GW**; statistical analysis: AN; drafting of the manuscript: **FJ**, **AN**; data interpretation and critical revision of the manuscript for valuable intellectual content: **AN**, **FJ**, **FB**, **LP**, **CC**, **PBJ**, **SL**, **GL**, **MM**, **KS**, **AVG**, **GW**; study supervision: **FJ**, **AN**, **FB**, **LP**.

Conflicts of interest

KS declares honoraria from BBraun, Fresenius Kabi, and being member of the board of the Polish Society of Enteral, Parenteral Nutrition and Metabolism. All other authors declare no conflict of interest.

References

[1] Pironi L, Boeykens K, Bozzetti F, Joly F, Klek S, Lal S, et al. ESPEN guideline on home parenteral nutrition. Clin Nutr 2020;39(6):1645–66.
[2] Staun M, Pironi L, Bozzetti F, Baxter J, Forbes A, Joly F, et al. ESPEN Guidelines on Parenteral Nutrition: home parenteral nutrition (HPN) in adult patients. Clin Nutr 2009;28(4):467–79.
[3] Schiffer CA, Mangu PB, Wade JC. Camp-Sorrell D, Cope DG, El-Rayes BF, et al. Central venous catheter care for the patient with cancer: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol 2013;31(10):1357–70.

[4] Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. Clin Infect Dis 2009;49(1):1–45.
[5] Pittiruti M, Hamilton H, Biffi R, MacFie J, Pertkiewicz M, Espen. ESPEN Guidelines on Parenteral Nutrition: central venous catheters (access, care, diagnosis and therapy of complications). Clin Nutr 2009;28(4):365–77.
[6] Pironi L, Arends J, Bozzetti F, Cuerda C, Gillanders L, Jeppesen PB, et al. ESPEN guidelines on chronic intestinal failure in adults. Clin Nutr 2016;35(2):247–307.
[7] Gompelman M, Paus C, Bond A, Akkermans RP, Bleeker-Rovers CP, Lal S, et al. Comparing success rates in central venous catheter salvage for catheter-related bloodstream infections in adult patients on home parenteral nutrition: a systematic review and meta-analysis. Am J Clin Nutr 2021;114(3):1173–88.
[8] Dreesen M, Foulon V, Spriet I, Goossens GA, Hiele M, De Pourcq L, et al. Epidemiology of catheter-related infections in adult patients receiving home parenteral nutrition: a systematic review. Clin Nutr 2013;32(1):16–26.
[9] O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis 2011;52(9):e162–93.
[10] Raad I, Hanna H, Maki D. Intravascular catheter-related infections: advances in diagnosis, prevention, and management. Lancet Infect Dis 2007;7(10):645–57.
[11] Liang SY, Marschall J. Update on emerging infections: news from the Centers for Disease Control and Prevention. Vital signs: central line-associated blood stream infections-United States, 2001, 2008, and 2009. Ann Emerg Med 2011;58(5):447–51.